ACRYLONITRILE
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 71 (1999) (p. 43)

CAS No.: 107-13-1
Chem. Abstr. Name: 2-Propenenitrile

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Acrylonitrile is a monomer used in high volume principally in the manufacture of acrylic fibres, resins (acrylonitrile–butadiene–styrene, styrene–acrylonitrile and others) and nitrile rubbers (butadiene–acrylonitrile). Other important uses are as an intermediate in the preparation of adiponitrile (for nylon 6/6) and acrylamide and, in the past, as a fumigant. Occupational exposures to acrylonitrile occur in its production and use in the preparation of fibres, resins and other products. It is present in cigarette smoke and has been detected rarely and at low levels in ambient air and water.

5.2 Human carcinogenicity data

The potential carcinogenicity of acrylonitrile in occupationally exposed populations has been investigated in several epidemiological studies. Studies carried out in the 1970s and 1980s suggested a possible increased risk of lung cancer among workers exposed to acrylonitrile. However, these were inconclusive because of one or more of the following actual or potential problems: small sample sizes, insufficient length of follow-up, incompleteness of follow-up, inadequate exposure assessment, potential confounding by other occupational carcinogens, and potential confounding by smoking. Consequently, larger and better studies were undertaken, in most cases building upon the same cohorts that had previously been assembled. Four such studies (two in the United States, one in the United Kingdom and one in the Netherlands) were carried out and these now provide the most relevant, informative data on which to base an evaluation. All of the studies made some attempt to establish exposure levels, although for the British study, this was rather cruder than for the others. The two studies from the United States were carried out in similar industries, but the range of cumulative exposure values was quite different between the two, raising questions about the inter-study comparability of methods of exposure assessment. The four studies employed different strategies for comparing exposed with unexposed. While the British study used a classic SMR comparison with national rates, the Dutch study did the same, but also compared the exposed with a different unexposed cohort. One of the studies from the United States compared the exposed with national rates and with rates of mortality and incidence in other plants of the same large company. The other compared the exposed with workers in the same plants who were unexposed to acrylonitrile. Typically, in each study, a number of analyses were carried out, varying comparison groups and other parameters.

There was no significant excess risk for any type of cancer when all exposed workers were compared with unexposed, or with an external comparison population. Further, when the study subjects were

subdivided by levels of exposure (cumulative exposure when feasible), for no site but lung was there any hint that risk increased with exposure. For lung cancer, there was an indication that workers with the highest exposures had relative risk estimates greater than 1.0. This finding was strongest in the largest of the studies, which had one of the most intensive exposure assessment protocols, but the other studies gave either negative or only weakly supportive results. Even in the largest study (where the relative risk in the highest exposure quintile ranged from 1.2 to 1.7 depending on the parameters in the analysis), the finding was not consistently statistically significant; there was no coherent dose–response pattern throughout the range of exposures and the risk in the highest decile of exposure was lower than that in the second highest decile. On balance and given the largely unsupportive findings from the other studies, the evidence from this one study was not considered to be sufficiently strong to conclude that there was a credible association between acrylonitrile and lung cancer. Thus, the earlier indications of an increased risk among workers exposed to acrylonitrile were not confirmed by the recent, more informative studies.

5.3 Animal carcinogenicity data

Acrylonitrile has been tested for carcinogenicity in one study in rats by inhalation with pre- and postnatal exposure. This study confirmed the findings of increased incidences of glial cell tumours of the central nervous system found in several previous studies that had not been fully reported and also found increases in malignant mammary tumours, Zymbal gland carcinomas, benign and malignant hepatocellular tumours and extrahepatic angiosarcomas.

5.4 Other relevant data

Acrylonitrile forms adducts with proteins and glutathione. It also forms DNA adducts *in vitro*, but only after cytochrome P450 bioactivation, most likely through its epoxide metabolite (cyanoethylene oxide), which is also formed *in vivo*. Acrylonitrile–haemoglobin adducts have been detected in exposed workers.

Both acrylonitrile and cyanoethylene oxide can conjugate with glutathione, leading to detoxification of these reactive compounds. At high doses of acrylonitrile, as used in animal studies, glutathione in certain tissues may be depleted. Such glutathione depletion will probably not occur at low-level human exposure.

Acrylonitrile is mutagenic *in vitro*; in *Salmonella* systems, bioactivation (to cyanoethylene oxide) is required, but in *Escherichia coli* and in rodent systems, bioactivation by an added microsomal system is not required. The results of genotoxicity experiments *in vivo* have in most cases been negative, although acrylonitrile is mutagenic in *Drosophila*.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of acrylonitrile.

There is *sufficient evidence* in experimental animals for the carcinogenicity of acrylonitrile.

Overall evaluation

Acrylonitrile is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluations: Vol. 19 (1979) (Acrylonitrile and copolymers); Suppl. 7 (1987)

Synonyms

- AN
- Cyanoethylene
- Propenenitrile
- VCN
- Vinyl cyanide

Last updated: 12 April 1999